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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/074,976	02/13/2002	Robert J. Hariri	011307	1042

20583 7590 09/20/2006

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 09/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/074,976	HARIRI, ROBERT J.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/3/06 has been entered.

The amendment, response, and declaration of Qian Ye, PhD are acknowledged. Claims 24, 27-29, 32-34, 41-43 have been amended, and claims 44-50 are newly submitted. Claims 24-50 are under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in the responses would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-43 stand rejected and claims 44-50 are newly rejected under the first paragraph of 35 U.S.C. 112 for reasons of record and following.

Although the declaration appears to be sufficiently persuasive to address the rejection of record, it was incomplete. The declaration mentioned seven figures, but only figures 4 and 6 are on record currently.

In section 22 of the declaration, Dr. Ye indicated that the CD34- placental stem cells are distinct from CD34- mesenchymal stem cells and cord blood stem cells in that they can develop embryoid-like bodies in cell culture.

In response, it is noted *Huss* review the state of the art of CD34- cells obtained from bone marrow and peripheral blood, and teaches that there exists a population of CD34- cells having surprising plasticity to the extend of totipotency (e.g. abstract), and states, "THE LASTEST DEVELOPMENT SHOW THAT THE POTENTIAL OF CD34- STEM CELLS IS ALMOST UNLIMITED TO GENERATE WHOLE ORGAN SYSTEMS WITH THIS TOTIPOTENT CELL POPULATION" (column 1, page 791). This teach provides evidence contrary to Dr. Ye's assertion on the distinction of placental CD34- stem cells and CD34- mesenchymal stem cells because a totipotent stem cell should be able to generate embryoid or embryoid-like bodies.

Accordingly, for reasons set forth *supra*, the rejection stands.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-31, 35-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 is vague and indefinite because of the claim recitation, "flush". The specification fails to define the condition for "flush", it is unclear what step(s) are encompassed by "flush", and thus the metes and bounds of the claims are uncertain.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 24-27, 31-36 stand or newly rejected under 35 U.S.C. 102(e) as being anticipated by *Pykett et al* (USP 6,548,299), for reasons of record and following.

In the Remarks, the applicant assert they have amended claim 24 to include draining and flushing steps, and thus obviate the rejection.

In response, claim 24 as amended only states the source of stem cells, i.e. from a human placenta, it does not require performing the steps of draining and flushing placenta, and thus the amendment dose not obviate the rejection.

Pykett et al teach a method of producing a three-dimensional matrix scaffold seeded with CD34+ hematopoietic progenitor cells, and the tissue matrix generated by the method; wherein the CD34+ cells may be collected from the cord blood (e.g. column 33, line 14), wherein the matrix tissue may be artificial or natural (e.g. column 9, line 61), and wherein the tissue lacking cells (decellularized), and preferably coated with

biological substances such as fibronectins and glycosaminoglycans to promote cell adhesion, migration, and growth (e.g. column 10, lines 10-35). Since the CD34+ cells collected from a placenta would not distinquish from those collected from a cord blood, accordingly, *Pykett et al* anticipate instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 24, 26-28, 35-40 stand or newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Pykett et al* (USP 6,548,299), in view of *Goldstein et al* (USP 5,899,936), and *Atala* (USP 6,753,181).

The teaching of *Pykett et al* was discussed *supra*. *Pykett et al* do not teach the ratio of the fibronectin to heparin, nor the details of how the stem cells are seeded on the matrices, nor the process of decellularization of a natural tissue/organ.

Goldstein et al and *Atala* supplemented *Pykett et al* by establishing that it was well known in the art the optimal ratio of the fibronectin to heparin for coating a bioprosthesis ranges from 0.1:1 to 10:1 (e.g. column 9, lines 7-17) and the process of decellularization of a natural tissue for making an implant. As to how the stem cells are seeded, *Pykett et al* do not literally state how this was done. However, given the state

of the art, the multiple means of seeding would have been common practice to one ordinary skilled in the art.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method taught by *Pykett et al, Goldstein et al*, and *Atala* by coating the matrices as taught by *Pykett et al* in an appropriate ratio of fibronectin to heparin as taught by *Goldstein et al* and decellularizing the matrix as taught by *Atala*, with a reasonable expectation of success. Given the state of the art, these limitations fall within the bound of optimization. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claim Rejections - 35 USC § 102/103

Claims 41-43 stand rejected and claims 44-50 are newly rejected under 35 U.S.C. 102(e) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over *Anderson et al* (USP 6,328,762) and as evidenced by *Huss et al* (J Hematother Stem Cell Res 2000 Dec;9(6):783-93), for reasons of record and following.

Anderson et al teach a tissue matrix (porous prosthetic implant) seeded with cells including stem cells from bone marrow, and mesenchymal stem cells which comprises both CD34+ and CD34- stem cells (e.g. claims 1 and 3), and a method of making such for tissue repair (e.g. abstract). Although *Anderson et al* do not describe the surface markers of the bone marrow cells and mesenchymal stem cells, it was well known in the art that bone marrow comprises both CD34+ and CD34- stem cells, and mesenchymal stem cells are CD34- as evidenced by *Huss et al*. *Huss et al* also teaches that the

CD34- bone marrow cells contains a population of stem cells that are totipotent. Thus, *Anderson et al* anticipate or in the alternative as obvious over the instant claimed invention.

Applicant asserted that Anderson does not teach or suggest a tissue matrix comprising *placenta* stem cells, let alone CD34- stem cells.

In response, the claimed "human placental stem cells" comprises a mixture of various cell types including CD34+ hematopoietic stem cells, CD34- mesenchymal stem cells, and a unique CD34- cell population described in the *Ye* declaration. Thus, given the broadest reasonable interpretation, seeding human placental stem cells into/onto a tissue matrix encompasses the conditions where only one or any two of the aforementioned populations are present in the matrix such as claimed in the instant claim 31. When the unique CD34-, CD45- cell population described in the *Ye* declaration is not present, the matrix product would be indistinguishable from the *Anderson* matrix product. *Anderson* teaches seeding bone marrow stem cells, which comprises either or both CD34+ and CD34- cells. Thus, so long as the tissue matrix taught by *Anderson et al* meet structural limitation containing a matrix plus CD34+ and/or CD34- stem cells, the claimed invention as a whole was at least *prima facie* obvious, if not anticipated, by the references, in the absence of sufficient, clear and convincing evidence to the contrary.

Applicant then argue that Ye declaration explains that placenta stem cells used in the present invention are different from bone marrow-derived stem cells, mesenchymal stem cells or embryonic stem cells.

In response, as an initial matter, it is noted, the *Ye* declaration states the CD34- placenta stem cells differ from hematopoietic, embryonic stem cells, cord blood-derived cells, or CD34- mesenchymal stem cells. However, it does not discuss bone marrow derived CD34- cells. There is no evidence on record that bone marrow does not contain the specific cell population described in the *Ye* declaration, nor there is evidence on record that CD34- stem cells isolated from a placenta does not contain CD34- mesenchymal stem cells found in the bone marrow. Particularly considering what has been taught in *Huss* review, "THE LASTEST DEVELOPMENT SHOW THAT THE POTENTIAL OF CD34- STEM CELLS [of bone marrow] IS ALMOST UNLIMITED TO GENERATE WHOLE ORGAN SYSTEMS WITH THIS TOTIPOTENT CELL POPULATION" (column 1, page 791). Thus, simply claiming "CD34- placenta stem cells" does not appear to exclude the CD34- cell population taught by *Anderson et al* in the absence of clear and convincing evidence.

As to the CD34- placenta stem cell population described in the declaration, it appears to contain a distinct stem cell population defined by a unique set of cell surface markers as recited in claims 29 and 30. However, this does not exclude the presence of classic CD34- mesenchymal stem cells and even the totipotent stem cells as seen in the bone marrow. Thus instant claims still encompass the scenario where the matrix are seeded with CD34+ stem cells and/or classic CD34- mesenchymal stem cells the same as from bone marrow, and thus anticipated by the cited art.

Claim Objections

Claims 29 and 30 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claim is allowed. It is noted placental stem cells as defined by claims 29 and 30 appear to be free of cited art of record.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Dave T. Nguyen** can be reached on 571-272-0731. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **William Phillips**, whose telephone number is (571) 272-0548.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
September 14, 2006